RECEIVED MR 57 5000 AUG 1 5 2000 sequence Listing TECH CENTER 1600/2900 eas Walter 0> Rufer, Sauer, Brian Lee <120 $\frac{1}{2}$  Method for Selecting Recombinase Variants with Altered Specificity <130> OMRF 178 <140> 09/544,045 <141> 2000 704-06 <150> 60/127,977 <151> 1999-04-09 <160> 68 <170> PatentIn Vèr. 2.1 <210> 1 <211> 343 <212> PRT <213> Artificial Sequênce : <220> <223> Description of Artificial Sequence: Cre <400> 1 Met Ser Asn Leu Leu Thr Val His Gln Asn Leu Pro Ala Leu Pro Val 10 Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val 35 Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu\Asn Asn Arg Lys Trp Phe 55 50 Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Lew Leu Tyr Leu Gln Ala

1

Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn

Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala

70

85

100 105 110

| Val        | Ser        | Leu<br>115 | Val        | Met        | Arg        | Arg        | Ile<br>120 | Arg        | Lys        | Glu        | Asn        | Val<br>125 | Asp        | Ala        | Gly        |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Glu        | Arg<br>130 | Ala        | Lys        | Gln        | Ala        | Leu<br>135 | Ala        | Phe        | Glu        | Arg        | Thr<br>140 | Asp        | Phe        | Asp        | Gln        |
| Val<br>145 | Arg        | Ser        | Leu        | Met        | Glu<br>150 | Asn        | Ser        | Asp        | Arg        | Cys<br>155 | Gln        | Asp        | Ile        | Arg        | Asn<br>160 |
| Leu        | Ala        | Phe        | Leu        | Gly<br>165 | Ile        | Ala        | Tyr        | Asn        | Thr<br>170 | Leu        | Leu        | Arg        | Ile        | Ala<br>175 | Glu        |
| Ile        | Ala        | Arg        | Ile<br>180 | Arg        | Val        | Lys        | Asp        | Ile<br>185 | Ser        | Arg        | Thr        | Asp        | Gly<br>190 | Gly        | Arg        |
| Met        | Leu        | Ile<br>195 | His        | Ile        | Gly        | Arg        | Thr<br>200 | Lys        | Thr        | Leu        | Val        | Ser<br>205 | Thr        | Ala        | Gly        |
| Val        | Glu<br>210 | Lys        | Ala        | Leu        | Ser        | Leu<br>215 | Gly        | Val        | Thr        | Lys        | Leu<br>220 | Val        | Glu        | Arg        | Trp        |
| Ile<br>225 | Ser        | Val        | Ser        | Gly        | Val<br>230 | Ala        | Asp        | Asp        | Pro        | Asn<br>235 | Asn        | Tyr        | Leu        | Phe        | Cys<br>240 |
| Arg        | Val        | Arg        | Lys        | Asn<br>245 | Gly        | Val        | Ala        | Ala        | Pro<br>250 | Ser        | Ala        | Thr        | Ser        | Gln<br>255 | Leu        |
| Ser        | Thr        | Arg        | Ala<br>260 | Leu        | Glu        | Gly        | Ile        | Phe<br>265 | Glu        | Ala        | Thr        | His        | Arg<br>270 | Leu        | Ile        |
| Tyr        | Gly        | Ala<br>275 | Lys        | Asp        | Asp        | Ser        | Gly<br>280 | Gln        | Arg        | Tyr        | Leu        | Ala<br>285 | Trp        | Ser        | Gly        |
| His        | Ser<br>290 | Ala        | Arg        | Val        | Gly        | Ala<br>295 |            | Arg        | Asp        | Met        | Ala<br>300 |            | Ala        | Gly        | Val        |
| Ser<br>305 | Ile        | Pro        | Glu        | Ile        | Met<br>310 |            | Ala        | Gly        | Gly        | Trp        | Thr        | Asn        | Val        | Asn        | Ile<br>320 |
| Val        | Met        | Asn        | Tyr        | 11e<br>325 |            | Asn        | Leu        | Asp        | Ser<br>330 |            | Thr        | Gly        | Ala        | Met<br>335 | Val        |

Arg Leu Leu Glu Asp Gly Asp 340

| <210>     | 2   |    |
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| <211>     | 13  |    |
| <212>     | DNA   |    |
| <213>     | Artificial Sequence                             |    |
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| <223>     | Description of Artificial Sequence: Inverted    |    |
|           | Repeat Sequence                                 |    |
|           |   |    |
| <220>     |   |    |
|           | N at sites 1-3 and 6-7 is either A, T, G or C   |    |
|           |   |    |
| <400>     | 2.  |    |
|           | nncgt ata                                       | 13 |
| 111111401 | oge add   |    |
|           |   |    |
| <210>     | 3   |    |
| <211>     |   |    |
| <212>     |   |    |
|           | Artificial Sequence                             |    |
| \213/     | Artificial dequence                             |    |
| <220>     |   |    |
|           | Description of Artificial Sequence: variant lox |    |
| <223>     | sites   |    |
|           | sices   |    |
| <b>.</b>  |   |    |
| <220>     | N at sites 1-3, 6-7, 14-21, 28-29, and 32-34 is |    |
| <223>     |   |    |
|           | either A, G, C, or T                            |    |
|           |   |    |
| <400>     |   | 34 |
| nnnac     | nnegt atannnnnnn ntataegnng tnnn                |    |
|           |   |    |
|           |   |    |
| <210>     |   |    |
| <211>     |   |    |
| <212>     |   |    |
| <213>     | Artificial Sequence                             |    |
|           |   |    |
| <220>     |   |    |
| <223>     | Description of Artificial Sequence: variant lox |    |
|           | sites   |    |
|           |   |    |
| <400>     |   | 33 |
| gatac     | caacgt atataccttt ctatacgttg tat                | J. |
|           |   |    |
|           |   |    |
| <210>     |   |    |
| <211>     | > 34  |    |

|           | ·   |    |
|-----------|---|----|
| <212>     | DNA   |    |
| <213>     | Artificial Sequence   |    |
|           |   |    |
| <220>     |   |    |
| <223>     | Description of Artificial Sequence: Specific and                                  |    |
|           | Non-specific sequences for Cre recombinase  |    |
|           |   |    |
| <220>     | 20 74 is either A C C   |    |
| <223>     | N at sites 1-3, 14-21, or 32-34 is either A, G, C, $\left(\frac{1}{2}\right)^{2}$ |    |
|           | or T  |    |
| . 4 0 0 . | -   |    |
| <400>     | ttogt atannnnnnn ntatacgaag tnnn  | 34 |
| nnnac     | ttegt atamminin nearacyddy cimi.  |    |
|           |   |    |
| <210>     | 6   |    |
| <211>     |   |    |
| <212>     |   |    |
|           | Artificial Sequence   |    |
|           |   |    |
| <220>     | ,   |    |
| <223>     | Description of Artificial Sequence:   |    |
|           | Oligonucleotide   |    |
|           |   |    |
| < 400     | > 6   | 8  |
| atrvb     | pygc  | 0  |
|           |   |    |
| 010       |   |    |
| <210      |   |    |
| <211      |   |    |
|           | > DNA<br>> Artificial Sequence  |    |
| <213      | Altilitia seguense  |    |
| <220      | >   |    |
| <223      | > Description of Artificial Sequence: Primer                                      |    |
|           |   |    |
| <400      | > 7   |    |
| ataa      | cttcgt ataatgtatg ctatacgaag ttat   | 3  |
|           |   |    |
|           |   |    |
| <210      | 3 <   |    |
| <211      | > 29  |    |
|           | > DNA   |    |
| <213      | 8> Artificial Sequence  |    |
|           |   |    |
| <220      | )>  |    |
| <223      | 3> Description of Artificial Sequence: Primer                                     |    |

| <400> 8 aaataatcta gactgagtgt gaaatgtcc                        | 29 |
|--|----|
| <210> 9 <211> 31 <212> DNA <213> Artificial Sequence           |    |
| <220><br><223> Description of Artificial Sequence: primer      |    |
| <400> 9 atatataagc ttatcattta cgcgttaatg g                     | 31 |
| <210> 10<br><211> 33<br><212> DNA<br><213> Artificial Sequence |    |
| <220> <223> Description of Artificial Sequence: primer         |    |
| <400> 10 ataagcggcc gctgagcttg gctgttttgg cgg                  | 33 |
| <210> 11<br><211> 36<br><212> DNA<br><213> Artificial Sequence |    |
| <220><br><223> Description of Artificial Sequence: primer      |    |
| <400> 11<br>gccgtctcga gagagtttgt agaaacgcaa aaaggc            | 3  |
| <210> 12<br><211> 30<br><212> DNA<br><213> Artificial Sequence |    |
| <220><br><223> Description of Artificial Sequence: primer      |    |

| •  |     |
|--|-----|
| <400> 12   |     |
| gtcaagctag ctagcaggtt tcccgactgg   | 30  |
|  |     |
|  |     |
| <210> 13   |     |
| <211> 36   |     |
| <212> DNA  |     |
| <213> Artificial Sequence  |     |
|  |     |
| <220>  |     |
| <223> Description of Artificial Sequence: primer   |     |
|  |     |
| <400> 13   | 2.6 |
| acattgcggc cgcagatctc ctctagagtc gacctg  | 36  |
|  |     |
| <210> 14   |     |
| <211> 20   |     |
| <212> DNA  |     |
| <213> Artificial Sequence  |     |
| V213/ Altificial Sequence  |     |
| <220>  |     |
| <pre>&lt;223&gt; Description of Artificial Sequence: primer</pre>  |     |
|  |     |
| <400> 14   |     |
| tttgggctag cgaattcgag  | 20  |
|  |     |
|  |     |
| <210> 15   |     |
| <211> 20   |     |
| <212> DNA  |     |
| <213> Artificial Sequence  |     |
|  |     |
| <220>  |     |
| <223> Description of Artificial Sequence: primer   |     |
| .400. 15   |     |
| <400> 15   | 20  |
| tttgggccag ctaaacatgc  | ۷ ر |
|  |     |
| <210> 16   |     |
| <211> 16<br><211> 20   |     |
| <211> 20<br><212> DNA  |     |
| <213> Artificial Sequence  |     |
| and the second s |     |
| <220>  |     |
|  |     |

<223> Description of Artificial Sequence: primer

| <400> 16 cggtgggaga atgttaatcc   | 20  |
|--|-----|
| .010. 17   |     |
| <210> 17   |     |
| <211> 18<br><212> DNA  |     |
| <213> Artificial Sequence  |     |
| VZ107 Michigan Boquos  |     |
| <220>  |     |
| <223> Description of Artificial Sequence: prime                              | er  |
|  |     |
| <400> 17   |     |
| ggacacagtg cccgtgtc  | 18  |
|  |     |
|  |     |
| <210> 18   |     |
| <211> 21   |     |
| <212> DNA  |     |
| <213> Artificial Sequence  |     |
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| <pre>&lt;223&gt; Description of Artificial Sequence: prim</pre>              | er  |
|  |     |
| <400> 18   |     |
| totgogttot gatttaatot g  | 21  |
|  |     |
|  |     |
| <210> 19   |     |
| <211> 18   |     |
| <212> DNA  |     |
| <213> Artificial Sequence  |     |
| <220>  |     |
| <pre>&lt;223&gt; Description of Artificial Sequence: prim</pre>              | er  |
|  |     |
| <400> 19   |     |
| ccaggccagg tatctctg  | 18  |
|  |     |
|  |     |
| <210> 20   |     |
| <211> 22   |     |
| <212> DNA  |     |
| <213> Artificial Sequence  |     |
| <220>  |     |
| <pre>&lt;220&gt; &lt;223&gt; Description of Artificial Sequence: print</pre> | ner |
|  |     |

| <400> 20<br>gtacgtgaga tatctttaac cc                           | 22  |
|--|-----|
| <210> 21<br><211> 22<br><212> DNA<br><213> Artificial Sequence |     |
| <220> <223> Description of Artificial Sequence: primer         |     |
| <400> 21<br>ttgctggata gtttttactg cc                           | 22  |
| <210> 22<br><211> 45<br><212> DNA<br><213> Artificial Sequence |     |
| <220> <223> Description of Artificial Sequence: primer         |     |
| <400> 22<br>gctatcaact cgcgccctgg gagggatttt tgaagcaact catcg  | 45  |
| <210> 23<br><211> 45<br><212> DNA<br><213> Artificial Sequence |     |
| <220> <223> Description of Artificial Sequence: primer         |     |
| <400> 23 gagttgcttc aaaaatccct cccagggcgc gagttgatag ctggc     | 4 5 |
| <210> 24<br><211> 45<br><212> DNA<br><213> Artificial Sequence |     |
| <220> <223> Description of Artificial Sequence: primer         |     |

| <400> 24 gctatcaact cgcgccctgg cagggatttt tgaagcaact catcg     | 45  |
|--|-----|
| <210> 25<br><211> 45<br><212> DNA<br><213> Artificial Sequence |     |
| <220><br><223> Description of Artificial Sequence: primer      |     |
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| <210> 26 <211> 45 <212> DNA <213> Artificial Sequence          |     |
| <220><br><223> Description of Artificial Sequence: primer      |     |
| <220><br><223> N at sites 17-25 is either A, G, C, or T        |     |
| <400> 26 gctatcaact cgcgccnnnn nnnnnatttt tgaagcaact catcg     | 45  |
| <210> 27<br><211> 45<br><212> DNA<br><213> Artificial Sequence |     |
| <220><br><223> Description of Artificial Sequence: primer      |     |
| <220><br><223> N at sites 17-25 is either A, G, C, or T        |     |
| <400> 27 gagttgcttc aaaaatnnnn nnnnnggcgc gagttgatag ctggc     | 4 5 |
| <210> 28   |     |

<211> 1172

<212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: wtCre <400> 28 tttgggctag cgaattcgag ctcggtaccc ggggatcctc tagactgagt gtgaaatgtc 60 caatttactg accgtacacc aaaatttgcc tgcattaccg gtcgatgcaa cgagtgatga 120 ggttcgcaag aacctgatgg acatgttcag ggatcgccag gcgttttctg agcatacctg 180 gaaaatgett etgteegttt geeggtegtg ggeggeatgg tgeaagttga ataaceggaa 240 atggtttccc gcagaacctg aagatgttcg cgattatctt ctatatcttc aggcgcgcgg 300 tetggeagta aaaactatee ageaacattt gggeeageta aacatgette ategteggte 360 cgggctgcca cgaccaagtg acagcaatgc tgtttcactg gttatgcggc ggatccgaaa 420 agaaaacgtt gatgccggtg aacgtgcaaa acaggctcta gcgttcgaac gcactgattt 480 cgaccaggtt cgttcactca tggaaaatag cgatcgctgc caggatatac gtaatctggc 540 atttctgggg attgcttata acaccctgtt acgtatagcc gaaattgcca ggatcagggt 600 taaagatato toacgtactg acggtgggag aatgttaato catattggca gaacgaaaac 660 gctggttagc accgcaggtg tagagaaggc acttagcctg ggggtaacta aactggtcga 720 gcgatggatt tccgtctctg gtgtagctga tgatccgaat aactacctgt tttgccgggt 780 cagaaaaaat ggtgttgccg cgccatctgc caccagccag ctatcaactc gcgccctgga 840 agggattttt gaagcaactc atcgattgat ttacggcgct aaggatgact ctggtcagag 900 atacctggcc tggtctggac acagtgcccg tgtcggagcc gcgcgagata tggcccgcgc 960 tggagtttca ataccggaga tcatgcaagc tggtggctgg accaatgtaa atattgtcat 1020 gaactatatc cgtaacctgg atagtgaaac aggggcaatg gtgcgcctgc tggaagatgg 1080 cgattagcca ttaacgcgta aatgataagc ttggctgttt tggcggatga gagaagattt 1140 1172 tcagcctgat acagattaaa tcagaacgca ga <210> 29 <211> 1172 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: mxoxox1 <400> 29 tttgggctag cgaattcgag ctcggtaccc ggggatcctc tagactgagt gtgaaatgtc 60 caatttactg accgtacacc aaaatttgcc tgcattacct gtcgatgcaa cgagtgatga 120 ggttcgcaag aacctgatgg ccatgttcag ggatcgccag gcgttttctg agcatacctg 180 gaaaatgctt ctgtccgttt gccggtcgtg ggcggcatgg tgcaagttga ataaccggaa 240 atggtttccc gcagaacctg aagatgttcg cgattatctt ctatatcttc aggcgcgcgg 300 tetggeagta aaaactatee ageaacattt gggeeageta aacatgette ategteggte 360 cgggctgcca cgaccaagtg acagcaatgc tgtttcactg gttatgcggc ggatccgaaa 420 agaaaacgtt gatgccggtg aacgtgcaaa acaggctcta gcgttcgaac gcactgattt 480 cgaccaggtt cgttcactca tggaaaatag cgatcgctgc caggatatac gtaatctggc 540 atttctgggg attgcttata acaccctgtt acgtatagcc gaaattgcca ggatcagggt 600

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taaagatato toacgtacta acggtgggag aatgttaato catattggca gaacgaaaac 660
gctggttagc accgcaggtg tagagaaggc acttagtctg ggggtaacta aactggtcga 720
gcgatggatt tccatctctg gtgtagctga tgatccgaat aactacctgt tttgccgggt 780
cagaaaaaat ggtgttgccg cgccatctgc caccagccag ctatcaactc gcgccctggg 840
agggattttt gaagcaacte ategattgat ttaeggeget aaggatgaet etggteagag 900
atacctggcc tggtctggac acagtgcccg tgtcggagcc gcgcgagata tggcccgcgc 960
tggagtttca ataccggaga tcatgcaagc tggtggctgg accaatgtaa atattgtcat 1020
gaactatatc cgtaacctgg atagtgaaac aggggcaatg gtgcgcctgc tggaagatgg 1080
cgattagcca ttaacgcgta aatgataagc ttggctgttt tggcggatga gagaagattt 1140
tcagcctgat acagattaaa tcagaacgca ga
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ggttcgcaag aacctgatgg acatgttcag ggatcgccag gcgttttctg agcatacctg 180
gaaaatgett etgteegttt geeggtegtg ggeggeatgg tgeaagttga ataaceggaa 240
atggtttccc gcagaacctg aagatgttcg cgattatctt ctatatcttc aggcgcgcgg 300
tetggcagta aaaactatee agcaacattt gggccageta aacatgette ategteggte 360
egggetgeca egaceaagtg acageaatge tgtttcactg gttatgegge ggateegaaa 420
agaaaacgtt gatgccggtg aacgtgcaaa acaggctcta gcgttcggac gcactgattt 480
 cgaccaggtt cgttcactca tggaaaatag cgatcgctgc caggatatac gtaatctggc 540
 atttctgggg attgcttata acaccctgtt acgtatagcc gaaattgcca ggatcagggt 600
 taaagatato toacgtactg acggtgggag aatgttaato catattggca gaacgaaaac 660
 gctggttagc accgcaggtg tagagaaggc acttagcctg ggggtaacta aactggtcga 720
 gcgatggatt tccgtctctg gtgtagctga tgatccgaat aactacctgt tttgccgggt 780
 cagaaaaaat ggtgttgccg cgccatctgc caccggccag ctatcaactc gcgccctggg 840
 agggattttt gaagcaactc atcgattgat ttacggcgct aaggatgact ctggtcagag 900
 atacctggcc tggtccggac acagtgcccg tgtcggagcc gcgcgagata tggcccgcgc 960
 tggagtttca ataccggaga tcatgcaagc tggtggctgg tccaatgtaa atattgtcat 1020
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gaactatatc cgtaacctgg atagtgaaac aggggcaatg gtgcgcctgc tggaagatgg 1080 cgattagcca ttaacgcgta aatgataagc ttggctgttt tggcggatga gagaagattt 1140

<220>
<223> Description of Artificial Sequence: mxoxox3

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<210> 32 <211> 1172 <212> DNA <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mxoxox4

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ataccaggee tggtetggae acagtgeeeg tgteggagee gegegagata tggeeegege 960
tggagtttca ataccggaga tcatgcaagc tggtggctgg accaatgtaa atattgtcat 1020
gaactatatc cgtaacctgg atagtgaaac aggggcaatg gtgcgcctgc tggaagatgg 1080
cgattagcca ttaacgcgta aatgataagc ttggctgttt tggcggatga gagaagattt 1140
                                                                  1172
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<210> 33
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<213> Artificial Sequence
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ggttcgcaag aacctgatgg ccatgttcag ggatcgccag gcgttttctg agcatacctg 180
gaaaatgctt ctgtccgttt gccggtcgtg ggcggcatgg tgcaagttga ataaccggaa 240
atggtttccc gcagaacctg aagatgttcg cgattatctt ctatatcttc aggcgcgcgg 300
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cgaccaggtt cgttcactca tggaaaatag cgatcgctgc caggatatac gtaatctggc 540
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gctggttagc accgcaggtg tagagaaggc acttagcctg ggggtaacta aacaggtcga 720
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Cont

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Och Cont

Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe 50 55 60

Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala 65 70 75 80

Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn

Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala Val Ser Leu Val Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly Glu Arg Ala Lys Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln Val Arg Ser Leu Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn Leu Ala Phe Leu Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu Ile Ala Arg Ile Arg Val Lys Asp Ile Ser Arg Thr Asn Gly Gly Arg Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp Ile Ser Ile Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu Ser Thr Arg Ala Leu Gly Gly Ile Phe Glu Ala Thr His Arg Leu Ile 

His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 

Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly 

Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile 

Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 

Arg Leu Leu Glu Asp Gly Asp

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Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly 195 200 205 Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp 215 Ile Ser Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys 225 230 235 Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Gly Gln Leu 245 250 Ser Thr Arg Ala Leu Gly Gly Ile Phe Glu Ala Thr His Arg Leu Ile 260 265 270 Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly 275 280 285 His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 295 Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile 310 315 Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 325 330 Arg Leu Leu Glu Asp Gly Asp 340 <210> 37 <211> 343 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: mxoxox3

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Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg 20 25 30

Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val 35 40 45 Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe 55 Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala 70 Arq Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn 90 85 Met Leu His Arq Arq Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala 105 Val Ser Leu Val Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly 120 125 Glu Arg Ala Lys Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln 130 135 Val Arg Ser Leu Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn 145 150 155 Leu Ala Phe Leu Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu 165 170 Ile Ala Arg Ile Arg Val Lys Asp Ile Ser Arg Thr Asn Gly Gly Arg 185 180 Met Leu Ile His Ile Ser Arg Thr Lys Thr Leu Val Ser Thr Ala Gly 200 205 Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Gln Trp 210 215 Ile Ser Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys 230 225 Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Arg Leu 245 250 Ser Thr Arg Ala Leu Gly Gly Ile Phe Glu Ala Thr His Arg Leu Ile

and Carl

Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly 275 280 285

265

His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 290 295 300 Ser Ile Leu Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile 305 310 315 320

Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 325 330 335

Arg Leu Leu Glu Asp Gly Asp 340

<210> 38

<211> 343

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mxoxox4

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Met Ser Asn Leu Leu Thr Val His Gln Asn Leu Pro Ala Leu Pro Val 1 5 10 15

Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg 20 25 30

Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val

Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe
50 55 60

Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Cys Leu Gln Ala
65 70 75 80

Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn 85 90 95

Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala 100 105 110

Val Ser Leu Val Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly
115 120 125

Glu Arg Ala Lys Gln Ala Leu Ala Phe Lys Arg Thr Asp Phe Asp Gln 130 135 140

Val Arg Ser Leu Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn

and

Leu Ala Phe Leu Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu 165 170 175

Ile Ala Arg Ile Arg Val Lys Asp Ile Ser Arg Thr Asp Gly Gly Arg
180 185 190

Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly
195 200 205

Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp 210 215 220

Ile Ser Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys 225 230 230 235 235

Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu 245 250 255

Ser Thr Arg Ala Leu Glu Gly Ile Phe Glu Ala Thr His Arg Leu Ile 260 265 270

Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Gln Ala Trp Ser Gly 275 280 285

His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 290 295 300

Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Thr Asn Val Asn Ile 305 310 315 320

Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 325 330 335

Arg Leu Leu Glu Asp Gly Asp 340

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<211> 343

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mxoxox5

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Ser Thr Arg Ala Leu Gly Gly Ile Phe Glu Ala Thr His Arg Leu Ile 265

Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Leu Ala Trp Ser Gly 275

His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 290 295 300

Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Ser Asn Val Asn Ile 305 310 315 320

Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val 325 330 335

Arg Leu Leu Glu Asp Gly Asp 340

<210> 40

<211> 343

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: mxoxox6

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Asp Ala Thr Ser Asp Glu Val Arg Lys Asn Leu Met Asp Met Phe Arg 20 25 30

Asp Arg Gln Ala Phe Ser Glu His Thr Trp Lys Met Leu Leu Ser Val 35 40 45

Cys Arg Ser Trp Ala Ala Trp Cys Lys Leu Asn Asn Arg Lys Trp Phe 50 60

Pro Ala Glu Pro Glu Asp Val Arg Asp Tyr Leu Leu Tyr Leu Gln Ala 65 70 75 80

Arg Gly Leu Ala Val Lys Thr Ile Gln Gln His Leu Gly Gln Leu Asn
85 90 95

Met Leu His Arg Arg Ser Gly Leu Pro Arg Pro Ser Asp Ser Asn Ala 100 105 110 Val Ser Leu Val Met Arg Arg Ile Arg Lys Glu Asn Val Asp Ala Gly Glu Arg Ala Lys Gln Ala Leu Ala Phe Glu Arg Thr Asp Phe Asp Gln Val Arg Ser Leu Met Glu Asn Ser Asp Arg Cys Gln Asp Ile Arg Asn Leu Ala Phe Leu Gly Ile Ala Tyr Asn Thr Leu Leu Arg Ile Ala Glu Ile Ala Arg Ile Arg Val Lys Asp Ile Ser Arg Thr Asp Gly Gly Arg Met Leu Ile His Ile Gly Arg Thr Lys Thr Leu Val Ser Thr Ala Gly Val Glu Lys Ala Leu Ser Leu Gly Val Thr Lys Leu Val Glu Arg Trp Ile Ser Val Ser Gly Val Ala Asp Asp Pro Asn Asn Tyr Leu Phe Cys Arg Val Arg Lys Asn Gly Val Ala Ala Pro Ser Ala Thr Ser Gln Leu Ser Thr Arg Ala Leu Gly Gly Ile Phe Glu Ala Thr His Arg Leu Ile Tyr Gly Ala Lys Asp Asp Ser Gly Gln Arg Tyr Gln Ala Trp Ser Gly His Ser Ala Arg Val Gly Ala Ala Arg Asp Met Ala Arg Ala Gly Val 

CM

325 330

Arg Leu Leu Glu Asp Gly Asp 340

<210> 41

Ser Ile Pro Glu Ile Met Gln Ala Gly Gly Trp Ser Asn Val Asn Ile

Val Met Asn Tyr Ile Arg Asn Leu Asp Ser Glu Thr Gly Ala Met Val

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ataacnncgt ata
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<400> 42
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ataacaacgt ata
<210> 43
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| < | <210> 45<br><211> 34<br><212> DNA<br><213> Artificial Sequence |    |
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|   | <400> 45 ataacaacgt atatacettt ctatagettg ttat                 | 34 |
| < | <210> 46 <211> 34 <212> DNA <213> Artificial Sequence          |    |
|   | <220><br><223> Description of Artificial Sequence: loxK1       |    |
|   | <400> 46<br>atacctttgt atataccttt ctatagaaag gtat              | 34 |
| < | <210> 47<br><211> 34<br><212> DNA<br><213> Artificial Sequence |    |
|   | <220><br><223> Description of Artificial Sequence: loxK2 'GG'  |    |
|   | <400> 47 ataacggcgt atataccttt ctatagcccg ttat                 | 34 |
| < | <210> 48 <211> 34 <212> DNA <213> Artificial Sequence          |    |
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| <211> 34  |     |
| <212> DNA<br><213> Artificial Sequence                |     |
| V213/ Altificial Sequence                             |     |
| <220>   |     |
| <223> Description of Artificial Sequence: lox K2 'TC' |     |
| •   |     |
| <400> 49  |     |
| ataactccgt atataccttt ctatagcgag ttat                 | 34  |
|   |     |
| (210) 50  |     |
| <210> 50<br><211> 34                                  |     |
| <212> DNA   |     |
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|   |     |
| <220>   |     |
| <223> Description of Artificial Sequence: lox K2 'GT' |     |
|   |     |
| <400> 50  |     |
| ataacgtcgt atataccttt ctatagcacg ttat                 | 34  |
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| <210> 51  |     |
| <211> 34  |     |
| <212> DNA   |     |
| <213> Artificial Sequence                             |     |
|   |     |
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| <223> Description of Artificial Sequence: lox K2 'TG' |     |
| <400  |     |
| <400> 51 ataactgcgt atataccttt ctatagccag ttat        | o : |
| acaaoogoge acacaoocci ocatagocag ccac                 | 34  |
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| <210> 52  |     |
| <211> 34  |     |
| <212> DNA   |     |
| <213> Artificial Sequence                             |     |
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| <223> Description of Artificial Sequence: LoxP        |     |

| <400> 52 ataacttcgt ataatgtatg ctatacgaag ttat                                  | 34       |
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| <210> 53 <211> 34 <212> DNA <213> Artificial Sequence                           |          |
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| <400> 53 gagcctttgt atataccttt ctatacaaag gctt                                  | 34       |
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| <220> <223> Description of Artificial Sequence: lox K2                          |          |
| <400> 54 gatacaacgt atataccttt ctatacgttg tatt                                  | 34       |
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| <220> <223> Description of Artificial Sequence: Gene                            |          |
| <400> 55 gctagcgaat tcgagcttcg gtacccgggg atcctctaga gtcgacctgc aggcatgcaa gctt | 60<br>64 |
| <210> 56 <211> 33 <212> DNA <213> Artificial Sequence                           |          |
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## oligonucleotide

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| <211> 00  |                                   |            |
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| ol        | igonucleotide                     |            |
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| <212> DN. |                                   |            |
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| ol        | igonucleotide                     |            |
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| <211> 35  |                                   |            |
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| <220>     |                                   |            |
|           | scription of Artificial Sequence: |            |
| ol.       | igonucleotide                     |            |
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| <213>          | Artificial Sequence                       |           |      |
| <220>          |   |           |      |
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|                | oligonucleotide                           | •         |      |
| . 4 0 0 .      | 60  |           |      |
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| grarag         | ggaac ttc                                 |           | J. 4 |
|                |   |           |      |
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| \213/          | Artificial bequeince                      |           |      |
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|                | oligonucleotide                           |           |      |
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gaagtteeta tteegaagtt eetatte

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|          | oligonucleotide                |       |  |  |
| . 100-   |                                |       |  |  |
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| tctaga 6 |                                |       |  |  |
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| 12237    | oligonucleotide                | ence. |  |  |
|          | Oligonacieotiae                |       |  |  |
| <400>    | 65                             |       |  |  |
|          | tcata ttc                      | 13    |  |  |
| 55-      |                                |       |  |  |
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